

SEQUENCE LISTING

<110> CHANG, Y-H VETRO, J.A. MICKA, W.S.

<120> Dominant Negative Variants of Methionine Aminopeptidase
2 ("MetAP2") and Clinical Uses Therefor

<130> 16153-8007

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<170> PatentIn Ver. 2.0

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<211> 71

<212> PRT

<213> Human polylysine

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<213> Mouse polylysine

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Lys Lys Lys Ser Asn Val Lys Lys Ile
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Ser Ala Ala Gly Glu Gln Glu Pro Asp Lys Glu Ser Gly Ala Ser Val
Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu
Arg Asp Glu Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr
Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln
Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His
Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr
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Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Xaa Prc Thr Gly Cys Ser 210 215 220

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Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Xaa Phe Gly Thr His Ile 245 250 255

Ser Gly Arg Ile Ile Xaa Cys Ala Phe Thr Val Thr Phe Asn Pro Lys 260 265 270

Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile 275 280 285

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Gln Val Lys Pro Ile Arg Asn Xaa Asn Gly Xaa Ser Ile Gly Gln Tyr 325 330 335

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Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys 405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu 420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys 435 440 445

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Val Ser Ala Val Gln Gln Glu Leu Asp Lys Glu Ser Gly Ala Leu Val
Asp Glu Val Ala Lys Gln Leu Glu Ser Gln Ala Leu Glu Glu Lys Glu
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Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 385 390 395

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Xaa Thr Phe Gly Ser 355 360 365

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys 405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu . 420 425 430

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Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys
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Lys Lys Lys Ser Asn Val Lys Lys Ile Glu Leu Leu Phe Pro Asp 50 55 60

Gly Lys Tyr Pro Glu Gly Ala Trp Met Asp Tyr His Gln Asp Phe Asn 65 70 75 80

Leu Gln Arg Thr Thr Asp Glu Glu Ser Arg Tyr Leu Lys Arg Asp Leu 85 90 95

Glu Arg Ala Glu His Trp Asn Asp Val Arg Lys Gly Ala Glu Ile His 100 105 110

Arg Arg Val Arg Arg Ala Ile Lys Asp Arg Ile Val Pro Gly Met Lys 115 120 125

Leu Met Asp Ile Ala Asp Met Ile Glu Asn Thr Thr Arg Lys Tyr Thr 130 135 140

Gly Ala Glu Asn Leu Leu Ala Met Glu Asp Pro Lys Ser Gln Gly Ile 145 150 155 160

Gly Xaa Pro Thr Gly Leu Ser Leu Asn His Cys Ala Ala Xaa Phe Thr 165 170 175

Pro Asn Ala Gly Asp Lys Thr Val Leu Lys Tyr Glu Asp Val Met Lys 180 185 190

Val Xaa Tyr Gly Val Gln Val Asn Gly Asn Ile Ile Xaa Ser Ala Phe 195 200 205

Thr Val Ser Phe Asp Pro Gln Tyr Asp Asn Leu Leu Ala Ala Val Lys 210 215 220

Asp Ala Thr Tyr Thr Gly Ile Lys Glu Ala Gly Ile Asp Val Arg Leu 225 230 235 240

Thr Asp Ile Gly Glu Ala Ile Gln Glu Val Met Glu Ser Tyr Glu Val 245 250 255

Glu Ile Asn Gly Glu Thr Tyr Gln Val Lys Pro Cys Arg Asn Xaa Cys 260 265 270

Gly Xaa Ser Ile Ala Pro Tyr Arg Xaa Xaa Gly Gly Lys Ser Val Pro 275 280 285

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Glu Lys Tyr Leu Phe Ala Leu Asn Asn Leu Val Arg His Gly Leu Val
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                        375
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Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr

330

Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala , , 340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser 355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 370 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu 420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys
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Glu Ala Ala Lys Lys Lys Arg Arg Lys Lys Lys Gly Lys Gly Ala 35 40 45

Val Ser Ala Val Gln Gln Glu Leu Asp Lys Glu Ser Gly Ala Leu Val 50 55 60

Asp Glu Val Ala Lys Gln Leu Glu Ser Gln Ala Leu Glu Glu Lys Glu 65 70 75 80

Arg Asp Asp Asp Glu Asp Gly Asp Gly Asp Ala Asp Gly Ala Thr 85 90 95

Gly Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln 100 105 110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val 115 120 125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg 130 135 140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln 145 150 155 160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His 165 170 175 Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr 180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile 195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser 210 215 . 220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr 225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile 245 · 250 255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys 260 265 270

Tyr Asp Ile Leu Leu Thr Ala Val Lys Asp Ala Thr Asn Thr Gly Ile 275 280 285

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Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr 305 310 315 320

Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Pro Tyr 325 330 335

Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Glu Ala 340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser 355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys
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Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu 420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys 435 440 445

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Lys Lys Lys Ser Asn Val Lys Lys Ile Glu Leu Leu Phe Pro Asp 50 55 60

Gly Lys Tyr Pro Glu Gly Ala Trp Met Asp Tyr His Gln Asp Phe Asn 65 70 75 80

Leu Gln Arg Thr Thr Asp Glu Glu Ser Arg Tyr Leu Lys Arg Asp Leu 85 90 95

Glu Arg Ala Glu His Trp Asn Asp Val Arg Lys Gly Ala Glu Ile His 100 105 110

Arg Arg Val Arg Arg Ala Ile Lys Asp Arg Ile Val Pro Gly Met Lys 115 120 125

Leu Met Asp Ile Ala Asp Met Ile Glu Asn Thr Thr Arg Lys Tyr Thr 130 135 140

Gly Ala Glu Asn Leu Leu Ala Met Glu Asp Pro Lys Ser Gln Gly Ile 145 150 155 160

Gly Phe Pro Thr Gly Leu Ser Leu Asn His Cys Ala Ala His Phe Thr 165 170 175

Pro Asn Ala Gly Asp Lys Thr Val Leu Lys Tyr Glu Asp Val Met Lys 180 185 190

Val Asp Tyr Gly Val Gln Val Asn Gly Asn Ile Ile Asp Ser Ala Phe 195 200 205

Thr Val Ser Phe Asp Pro Gln Tyr Asp Asn Leu Leu Ala Ala Val Lys 210 215 220

Asp Ala Thr Tyr Thr Gly Ile Lys Glu Ala Gly Ile Asp Val Arg Leu 225 230 235 240

Thr Asp Ile Gly Glu Ala Ile Gln Glu Val Met Glu Ser Tyr Glu Val 245 250 255

Glu Ile Asn Gly Glu Thr Tyr Gln Val Lys Pro Cys Arg Asn Leu Cys 260 265 270

Gly His Ser Ile Ala Pro Tyr Arg Ile His Gly Gly Lys Ser Val Pro 275 280 285

Ile Val Lys Asn Gly Asp Thr Thr Lys Met Glu Glu Glu Glu His Phe 290 295 300

Ala Ile Glu Thr Phe Gly Ser Thr Gly Arg Gly Tyr Val Thr Ala Gly 305 310 315 320

Gly Glu Val Ser His Tyr Ala Arg Ser Ala Glu Asp His Gln Val Met 325 330 335

Pro Thr Leu Asp Ser Ala Lys Asn Leu Leu Lys Thr Ile Asp Arg Asn 340 345 350

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Phe Gly Thr Leu Pro Phe Cys Arg Arg Tyr Leu Asp Arg Leu Gly Gln
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Glu Lys Tyr Leu Phe Ala Leu Asn Asn Leu Val Arg His Gly Leu Val
Gln Asp Tyr Pro Pro Leu Asn Asp Ile Pro Gly Ser Tyr Thr Ala Gln
Phe Glu His Thr Ile Leu Leu His Ala His Lys Lys Glu Val Val Ser
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Lys Gly Asp Asp Tyr Gly Lys Met Arg Phe Gln Met Ala Ser Ser Leu
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Gly Ile Ile Leu Leu
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Val Ser Ala Gly Gln Gln Glu Leu Asp Lys Glu Ser Gly Thr Ser Val
Asp Glu Val Ala Lys Gln Leu Glu Arg Gln Ala Leu Glu Glu Lys Glu
                     70
Lys Asp Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Ala
Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Arg Val Gln
                                105
Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val
        115
Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg
Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln
                    150
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Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His 165 170 175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr 180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile 195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Xaa Pro Thr Gly Cys Ser 210 215 220

Leu Asn Asn Cys Ala Ala Xaa Tyr Thr Pro Asn Ala Gly Asp Thr Thr 225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Xaa Phe Gly Thr His Ile 245 250 255

Ser Gly Arg Ile Ile Xaa Cys Ala Phe Thr Val Thr Phe Asn Pro Lys 260 265 270

Tyr Asp Ile Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile 275 280 285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile 290 295 300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr 305 310 315 320

Gln Val Lys Pro Ile Arg Asn Xaa Asn Gly Xaa Ser Ile Gly Pro Tyr 325 330 335

Arg Xaa Xaa Ala Gly Lys Thr Val Pro Ile Val Lys Gly Glu Ala 340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Xaa Thr Phe Gly Ser 355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys 405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu 420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Xaa Pro Pro Xaa Cys 435 440 445

Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Xaa His Thr Ile Leu Cys 450 455 460

Ala Gln Pro Val Lys Lys Leu Ser Ala Glu Glu Met Thr Ile Lys Thr 465 470 475 480

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<400> 17

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Glu Ala Ala Lys Lys Lys Arg Arg Lys Lys Lys Gly Lys Gly Ala
35 40 45

Val Ser Ala Gly Gln Gln Glu Leu Asp Lys Glu Ser Gly Thr Ser Val 50 55 60

Asp Glu Val Ala Lys Gln Leu Glu Arg Gln Ala Leu Glu Glu Lys Glu 65 70 75 80

Lys Asp Asp Asp Glu Asp Gly Asp Gly Asp Gly Ala Ala 85 90 95

Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Arg Val Gln 100 105 110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val 115 120 125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg 130 135 140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln 145 150 155 160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His 165 170 175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr 180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile 195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser 210 215 220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr 225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile 245 250 255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys 260 265 270

Tyr Asp Ile Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile 275 280 285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile 290 295 300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr 305 310 315 320

Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Pro Tyr 325 330 335

Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala 345 Thr Arg Met Glu Glu Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser 360 Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 375 Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys 395 His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys 405 Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu 420 425 Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys 440 Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Glu His Thr Ile Leu Cys 455 Ala Gln Pro Val Lys Lys Leu Ser Ala Glu Glu Met Thr Ile Lys Thr 470 475 480

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gccacctgaa tcgcgacctg gatccagacg acagggaaga gggaacctcc agcacggccg 180
aggaagccgc caagaagaaa agacggaaga agaagaaggg caaaggggct gtgtcaqcag 240
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gtgatggtgc agctgggaag aagaagaaaa agaagaagaa gaagaggga ccaagagttc 420
aaacagaccc tccctcagtt ccaatatgtg acctgtatcc taatggtgta tttcccaaag 480
gacaagagtg tgaataccca cccacccaag atgggcggac agctgcttgg agaaccacaa 540
gtgaagagaa aaaggcgcta gaccaggcta gtgaggagat ttggaacgac ttccgagaag 600
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caattgggcc atatagaatt catgctggaa aaacagtgcc cattgtgaaa ggaggggaag 1140
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37

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